Complete Summary

GUIDELINE TITLE

VA/DoD clinical practice guideline for the management of dyslipidemia.

BIBLIOGRAPHIC SOURCE(S)

Management of Dyslipidemia Working Group. VA/DoD clinical practice guideline for the management of dyslipidemia. Washington (DC): Department of Veterans Affairs, Department of Defense; 2006. 140 p.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Veterans Health Administration, Department of Defense. VHA/DoD clinical practice guideline for the management of dyslipidemia in primary care. Washington (DC): Veterans Health Administration, Department of Defense; 2001 Dec. Various p.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references drugs for which important revised regulatory information has been released.

- March 2, 2005, Crestor (rosuvastatin calcium): Revisions to the WARNINGS, DOSAGE AND ADMINISTRATION, CLINICAL PHARMACOLOGY, and PRECAUTIONS sections of the labeling.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Dyslipidemia

GUIDELINE CATEGORY

Diagnosis
Management
Prevention
Screening
Treatment

CLINICAL SPECIALTY

Cardiology
Family Practice
Internal Medicine
Nutrition

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Dietitians
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To promote reduction of cardiovascular risk via evidence-based management of dyslipidemia, thereby improving clinical outcomes
- To assist primary care providers or specialists in the detection of high blood cholesterol, assessment of the global risk for cardiovascular disease (CVD), determination of treatment goals and appropriate therapies, and delivery of individualized interventions
- To incorporate information from several existing, national recommendations into a format that would maximally facilitate clinical decision-making

TARGET POPULATION

Adults (age 17 years or older) eligible for care in the Veterans Health Administration/Department of Defense (VHA/DoD) health care system

INTERVENTIONS AND PRACTICES CONSIDERED

Assessment/Diagnosis/Screening

1. Patient history and assessment of risk factors for cardiovascular disease
2. Measurement of total cholesterol and high-density lipoprotein (HDL) or total cholesterol (TC), high-density lipoprotein, triglycerides (TG), and low-density lipoprotein (LDL)
3. Fasting lipid profile, including low-density lipoprotein
4. Assessment of body mass index and waist circumference
5. Diagnosis of possible secondary causes of elevated low-density lipoprotein cholesterol using measurement of serum thyroid-stimulating hormone (TSH), blood urea nitrogen (BUN)/creatinine, liver function tests, and dipstick urinalysis
6. Assessment of baseline serum transaminases

Management/Treatment/Primary and Secondary Prevention

1. Age-appropriate lifestyle education on smoking, diet, and exercise
2. Non-pharmacological management, including therapeutic lifestyle changes (TLC), medical nutrition therapy (MNT), and exercise
3. Pharmacological therapy (monotherapy or combination therapy), including statins, niacin, resins, ezetimibe, fish oil/omega-3 fatty acids, n-3 polyunsaturated fatty acid (PUFA) supplements, fibrates
4. Addressing adherence to therapy and safety concerns
5. Repetition of dyslipidemia evaluation

MAJOR OUTCOMES CONSIDERED

- Total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglyceride levels
- Risk of developing coronary heart disease
- Risk of developing atherosclerotic cardiovascular disease
- Response to lifestyle changes and therapy, such as dietary changes, exercise, weight reduction, smoking cessation, reduction of excessive alcohol, and drug therapy
- Adherence to diet, exercise and drug therapy
- Cardiovascular disease outcomes (myocardial infarction, mortality, strokes)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Formulating of Questions

The Working Group developed researchable questions and associated key terms after orientation to the seed guideline and to goals that had been identified by the Working Group. The questions specified: (adapted from the Evidence-Based

Medicine [EBM] toolbox, Centre for Evidence-Based Medicine, [http://www.cebm.net]):

- Population - Characteristics of the target patient population
- Intervention - Exposure, diagnostic, or prognosis
- Comparison - Intervention, exposure, or control used for comparison
- Outcome - Outcomes of interest

These specifications served as the preliminary criteria for selecting studies. Research questions focused on the following areas of inquiry: screening, risk assessment, strategies, metabolic syndrome, non-drug therapy, drug monotherapy, drug combination therapy, and adverse effects.

Selection of Evidence

Published, peer-reviewed, randomized controlled trials (RCTs) were considered to constitute the strongest level of evidence in support of guideline recommendations. This decision was based on the judgment that RCTs provide the clearest, scientifically sound basis for judging comparative efficacy. The Working Group made this decision recognizing the limitations of RCTs, particularly considerations of generalizability with respect to patient selection and treatment quality. Evidence-based systematic reviews were considered to be the strongest level of evidence as well as meta-analyses that included randomized controlled studies. The evidence selection was designed to identify the best available evidence to address each key question and ensured maximum coverage of studies at the top of the hierarchy of study types: evidence-based guidelines, meta-analyses, and systematic reviews. When available, the search sought out critical appraisals already performed by others that described explicit criteria for deciding what evidence was selected and how it was determined to be valid. The sources that have already undergone rigorous critical appraisal include Cochrane Reviews, Best Evidence, Technology Assessment, and evidence-based practice center (EPC) reports.

The search was performed using the National Library of Medicine's (NLM) MEDLINE database. The term "hyperlipidemia" was used together with the following Boolean expressions and terms:

- Epidemiology
- Screening
- Diagnosis
- Primary Care
- Protocols
- Therapy
- Patient Education
- Economics

In addition to Medline/PubMed, the following databases were searched: Database of Abstracts of Reviews of Effectiveness (DARE) and Cochrane Central Register of Controlled Trials (CCTR). For Medline/PubMed searches, limits were set for language (English), date of publication (1999 through August 2004) and type of research (RCT and meta-analysis).

Once definitive reviews or clinical studies that provided valid relevant answers to the question were identified, the search ended. The search was extended to studies/reports of lower quality (observational studies) only if there were no high quality studies.

Exclusion criteria included reviews that omitted clinical course or treatment. Some retrieved studies were rejected on the basis of published abstracts, and a few were rejected after the researchers scanned the retrieved citation for inclusion criteria. Typical exclusions included studies with physiological endpoints or studies of populations that were not comparable to the population of interest (e.g., studies of dyslipidemia in children). The bibliographies of the retrieved articles were hand-searched for articles that may have been missed by the computer search. Working Group members also contributed articles as part of the evidence gathering process.

The results of the search were organized and evidence reports as well as copies of the original studies were provided to the Working Group for further analysis.

Literature Review and Inclusion Criteria

As a result of the original and updated literature reviews, articles were identified for possible inclusion. These articles formed the basis for formulating the guideline recommendations. The following inclusion criteria were used for selecting randomized controlled trial studies:

- Articles published between 1999 and 2004, with some exceptions
- English language only
- Full articles only
- Age limited to adults >18 years
- Minimum study size of 100 patients per arm
- Randomized controlled trials only; no cross-over trials
- Minimum 1 year for cardiovascular (CVD) outcomes (myocardial infarctions, mortality, strokes, etc.)
- Minimum 12 weeks for intermediate outcomes (total cholesterol, low-density lipoproteins [LDL], high-density lipoproteins, triglycerides)
- Baseline LDL levels reported
- Sufficient information to identify patient risk level
- Key outcomes cited

For some questions, special inclusion criteria (mostly related to minimum clinical trial size) were developed based upon research question content and available literature.

The literature search for the guideline update was validated by: (1) comparing the results to a search conducted by the independent research and appraisal team; (2) a review of the database by the expert panel; and (3) requesting articles pertaining to special topics from the experts in the Working Group. It is important to note that due to application of article screening criteria in the updated guideline, some of the studies that were included in the original guideline were not included in the updated analyses.

The guideline also drew heavily from the following sources for recommendations:

- Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on the detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). Journal of the American Medical Association 2001, 285 (19), 2486-2497.
- NCEP ATP-III, 2002: Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002, 106, (25), 3143-421.
- The U.S. Preventive Services Task Force Guide to Clinical Preventive Services. Second Edition 2001.
- Pharmacy Benefits Management—Medical Advisory Panel. The pharmacologic management of hyperlipidemia. VHA PBM-SHG Publication. Hines, IL: Pharmacy Benefits Management Strategic Health Group, Veterans Health Administration, Department of Veterans Affairs.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence

I: At least one properly done randomized controlled trial

II-1: Well designed controlled trails without randomization

II-2: Well designed cohort or case-control analytic study, preferably from more than one source

II-3: Multiple time series evidence with/without intervention; dramatic results of uncontrolled experiment

III: Opinion of respected authorities, descriptive studies, case reports, and expert committees

Overall Quality

Good: High grade evidence (I or II-1) directly linked to health outcome

Fair: High grade evidence (I or II-1) linked to intermediate outcome; or moderate grade evidence (II-2 or II-3) directly linked to health outcome

Poor: Level III evidence or no linkage of evidence to health outcome.

Net Effect of Intervention

Substantial:

- More than a small relative impact on a frequent condition with a substantial burden of suffering, or
- A large impact on an infrequent condition with a significant impact on the individual patient level

Moderate:

- A small relative impact on a frequent condition with a substantial burden of suffering, or
- A moderate impact on an infrequent condition with a significant impact on the individual patient level

Small:

- A negligible relative impact on a frequent condition with a substantial burden of suffering, or
- A small impact on an infrequent condition with a significant impact on the individual patient level

Zero or Negative:

- Negative impact on patients, or
- No relative impact on either a frequent condition with a substantial burden of suffering, or
- An infrequent condition with a significant impact on the individual patient level

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Preparation of Evidence Tables (Reports) and Evidence Rating

A group of research analysts, with experience in evidence-based appraisal, independently read and coded each article that met inclusion criteria. The research team prepared a brief summary of the critical appraisal of each article that included the following components:

- Description of patient population
- Interventions
- Comparisons
- Outcomes
- Summary of results
- Analysis of findings

- Evidence Appraisal
- Clinical significance

Quality of evidence ratings were assigned for each source of evidence using the grading scale presented in "Rating Scheme for the Strength of the Evidence" in this summary. The quality rating procedure used in this update was different from the rating scale used in the development of the original guideline in 1999. Where adjustments to the update process were made, articles from the original process were re-graded to reflect the changed rating scale (e.g., the Strength of Recommendation [SR] was assigned for each evidence, based on study design and significance of the quality of the evidence).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The development of the 2005 Dyslipidemia Guideline Update (version 2.0) was initiated in September 2004 and continued through November 2005. The development process followed the steps described in "Guideline for Guideline," an internal working document of Veterans Health Administration's (VHA's) National Clinical Practice Guideline Council, which requires an ongoing review of the work in progress. The 1999 Veterans Administration/Department of Defense (VA/DoD) Dyslipidemia Guideline represented a "seed document" that was updated and adapted by the joint VA/DoD Dyslipidemia Working Group. As with the original Working Group, the charge of the VA/DoD group was to provide evidence-based action recommendations whenever possible; hence, major clinical randomized controlled trials (RCTs) and observational studies published from August 1999 through August 2004 in the areas of diagnosis and treatment of dyslipidemia.

Guideline Development Process

The Offices of Quality and Performance and Patient Care Service, in collaboration with the network Clinical Managers, the Deputy Assistant Under Secretary for Health, and the Medical Center Command of the DoD identified clinical leaders to champion the guideline development process. During a preplanning conference call, the clinical leaders defined the scope of the guideline and identified a group of clinical experts from the VA and DoD that formed the Guideline Development Working Group. Working Group members included representatives of the following specialties: internal medicine, cardiology, endocrinology, medical nutrition therapy, social work, family practice, nursing, pharmacy, and rehabilitation medicine.

At the start of the update process, the clinical leaders, guideline Working Group members, outside experts, and experts in the field of guideline and algorithm development were consulted to determine which aspects of the 1999 guideline required updating. These consultations resulted in the following recommendations that guided the update efforts: (1) update any recommendations from the original guideline likely to be affected by new research findings; (2) provide information and recommendations on health systems changes relevant to dyslipidemia

screening and treatment; (3) address content areas and models of treatment for which little data existed during the development of the original guideline; and (4) review the performance and lessons learned since the implementation of the original guideline.

The Working Group participated in an initial face-to-face meeting to reach consensus about the guideline algorithm and recommendations and to prepare a draft document. The draft continued to be revised by the Working Group at-large through numerous conference calls and individual contributions to the document. Following the initial effort, an editorial panel of the Working Group convened to further edit the draft document. Recommendations for the performance or exclusion of specific procedures or services derived through a rigorous methodological approach that includes the following:

- Determination of appropriate criteria, such as effectiveness, efficacy, population benefit, or patient satisfaction
- Literature review to determine the strength of the evidence in relation to these criteria
- Formulation of the recommendations and grading of the level of evidence supporting the recommendation

Selection of Evidence

Each reference was appraised for scientific merit, clinical relevance, and applicability to the populations served by the Federal healthcare system. Recommendations were based on consensus of expert opinions and clinical experience only when scientific evidence was unavailable. Although the Strength of Recommendation (SR) rating was influenced primarily by the science, other factors were taken into consideration when assigning a SR rating such as: the burden of suffering imposed on the patient.

Recommendation and Overall Quality Rating

Evidence-based practice involves integrating clinical expertise with the bets available clinical evidence derived from systematic research. The Working Group received an orientation and tutorial on the evidence U.S. Preventive Services Task Force (USPSTF) 2001 rating process, reviewed the evidence, and independently formulated Quality of Evidence Ratings, a rating of Overall Quality, and a Net Effect of the Intervention (see "Rating Scheme for the Strength of the Evidence" in this summary) and a Final Grade of Recommendation (see "Rating Scheme for the Strength of the Recommendations" in this summary).

Lack of Evidence – Consensus of Experts

The majority of the literature supporting the science for these guidelines is referenced throughout the document and is based upon key RCTs and longitudinal studies published from 1999 through 2004. Following the independent review of the evidence, a consensus meeting was held to discuss discrepancies in ratings and formulate recommendations. Where existing literature was ambiguous or conflicting, or where scientific data was lacking on an issue, recommendations were based on the clinical experience of the Working Group. These

recommendations are indicated in the evidence tables as based on "Working Group Consensus.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

	Net Benefit of the Intervention			
Quality of Evidence	Substantial	Moderate	Small	Zero or Negative
Good	A	B	C	D
Fair	B	B	C	D
Poor	I	I	I	I

A: A strong recommendation that the clinicians provide the intervention to eligible patients.
Good evidence was found that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.

B: A recommendation that clinicians provide (the service) to eligible patients.
At least fair evidence was found that the intervention improves health outcomes and concludes that benefits outweigh harm.

C: No recommendation for or against the routine provision of the intervention is made.
At least fair evidence was found that the intervention can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.

D: Recommendation is made against routinely providing the intervention to asymptomatic patients.
At least fair evidence was found that the intervention is ineffective or that harms outweigh benefits.

I: The conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention.
Evidence that the intervention is effective is lacking, or poor quality, or conflicting and the balance of benefits and harms cannot be determined.

COST ANALYSIS

Published cost analyses were reviewed in the preparation of the guideline.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Experts from the Veterans Administration (VA) and Department of Defense (DoD) internal medicine, cardiology and primary care reviewed the final draft. Their feedback was integrated into the final draft.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The recommendations for the management of dyslipidemia in the primary care setting are organized into 3 major algorithms. Each algorithm, the objectives and recommendations that accompany it, and the evidence supporting the recommendations are presented below. The quality of evidence (QE) grading (I-III); overall quality (Good, Fair, Poor); and final grade of recommendations (R) (A-D, I) are provided for specific statements. These grades, along with "net effect of the interventions" are defined at the end of the "Major Recommendations" field.

Screening Algorithm

Note: A list of all abbreviations is provided at the end of the "Major Recommendations" field.

A. Adult Patient Enrolled in the Health Care System

Definition

This guideline addresses adults (age 17 years or older) eligible for care in the Veterans Health Administration/ Department of Defense (VHA/DoD) healthcare systems.

B. Does Patient Have a History of Cardiovascular Disease (CVD)?

Objective

Identify patients who may benefit from lipid lowering therapy.

Recommendations

1. All patients with known CVD are considered high-risk and should be treated with aggressive lipid-lowering therapy to prevent acute vascular events. These include, but are not limited to, acute myocardial infarction (AMI) or cerebrovascular accident (CVA).

C. Does Patient Have Diabetes Mellitus?

Objective

Identify patients known to be at high-risk due to diabetes mellitus (DM).

Recommendation

1. Patients with Type 2 DM are at significantly increased risk of CVD compared with non-diabetic patients of similar age and should, therefore, be treated more aggressively according to secondary prevention protocols. [A]

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Persons with Type-2 DM, even in the absence of CVD, should be treated as CVD equivalent	Haffner et al., 1998 Yusuf et al., 2000 Heart Protection Study Collaborative Group (HPS), 2002 Malmberg et al., 2000	I	Good	A

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

D. Assess Risk Factors for Cardiovascular Disease

Objective

Identify clinical markers that predict an increased risk for developing CVD, thereby changing the interpretation of low-density lipoprotein (LDL) levels.

Recommendations

1. Patients screened for dyslipidemia should be assessed for risk factors for CVD. Assessment should include, but not be limited to, the following:
    a. Age (males $\geq$age 45 and females $\geq$age 55)
    b. Family history of premature coronary artery disease; definite myocardial infarction (MI) or sudden death before age 55 in father or other male first-degree relative, or before age 65 in mother or other female first-degree relative
    c. Current tobacco use/cigarette smoking (or within the last month)
    d. Hypertension (systolic blood pressure $\geq$140 mmHg or diastolic blood pressure $\geq$90 mmHg confirmed on more than one occasion, or current therapy with anti-hypertensive medications)
    e. Diabetes mellitus (DM) (elevated fasting blood sugar [$\geq$126 mg/dL], or a random blood sugar [$\geq$200 mg/dL] confirmed on more than one occasion, an abnormal glucose tolerance test or current therapy with anti-diabetic medications)
    f. Level of high-density lipoprotein cholesterol (HDL-C) (less than 40 mg/dL confirmed on more than one occasion).

2. In obese patients (body mass index [BMI] $\geq$30), waist circumference measurement should be obtained to assist in the diagnosis of metabolic syndrome.

E. Lipid Screening Criteria

Objective

Appropriately target individuals for lipid profile screening.

Lipid Screening Criteria
1. Male age 35 or older OR female age 45 or older OR 2. Young adults with more than one of the following: a. Family history of premature CVD b. Patient is smoking c. Patient has or is being treated for hypertension 3. Consider obtaining lipid profile for young adults with abdominal obesity

Recommendations

1. Fasting lipid profile testing should be obtained in all men age 35 and older and women age 45 years or older every 5 years. [A]
2. Fasting lipid profile testing should be obtained in individuals with a family history or clinical evidence of familial hyperlipidemia. [A]
3. Fasting lipid profile testing in young adults may be considered depending upon the association with other risk factors. Younger adults (men younger than age 35 and women age 45 or younger) should be screened for lipid disorders if they have one or more of the following risk factors: family history of premature CVD, hypertension (or under treatment for hypertension [HTN]), or smoking. [B]
4. A lipid profile should be obtained for individuals with abdominal obesity (waist circumference >40 inches in men and >35 inches in women) to aid in assessment of metabolic syndrome. [B]
5. All persons with average or below average risk for atherosclerotic events should be screened for dyslipidemia every five years. [I]
6. Elderly patients age 75 or older should be screened if they have multiple CVD risk factors, or a history of CVD and good quality of life with no other major life-limiting diseases. [I]

The Recommended Screening Schedules for Dyslipidemia
For young adults (men <age 35; women <age 45) • Every 5 years when no CVD risk factors are present • More often, if family history of premature CVD exists (definite MI or sudden death before 55 years of age in father or other male first-degree relative or before age 65 in mother or other female first-degree relative) For middle-aged adults (men >age 35; women >age 45) • Every 5 years, when no CVD risk factors are present • Annually, if CVD risk factors exist (HTN, smoking, family history of premature CVD) For elderly patients up to age 75 years • Every 5 years when no CVD risk factors are present

The Recommended Screening Schedules for Dyslipidemia
• More often if CVD risk factors exist For elderly patients >age 75 • Evaluate if patient has multiple CVD risk factors, established CVD, or a history of revascularization procedures and good quality of life with no other major life-limiting diseases.

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Fasting lipid profile should be obtained in men ≥age 35 and women ≥age 45	Third Report of the National Cholesterol Education Program Expert Panel (NCEP) on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report (NCEP ATP-III), 2002 U.S. Preventive Services Task Force (USPSTF), 2001	I	Good	A
2	Fasting lipid profile should be obtained in patients with family history or clinical evidence of familial hyperlipidemia	NCEP ATP-III, 2002	I	Good	A
3	Consider screening fasting lipid profile in young adults with other risk factors (family history of premature CVD, HTN, or smoking)	NCEP ATP-III, 2002 Pignone et al., 2001 USPSTF, 2001 "A multicenter comparative trial," 1993	I	Fair	B
4	Fasting lipid profile should be obtained for patients with increased waist circumference (men >40 inches , women >35 inches) to aid in assessment of metabolic syndrome	NCEP ATP-III, 2002	I	Good	B
5	Persons with average or below average CV risk should be screened every five years	Working Group Consensus	III	Poor	I
6	Elderly patients age >75 should be screened if they have multiple CVD risk factors, a history of CVD and good quality of life with no other major life-limiting diseases	Working Group Consensus	III	Poor	I

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

F. Obtain a Fasting Lipid Profile

Objective

Screen appropriate patients for the presence of dyslipidemia.

Lipid Screening Test
• Ensure test obtained in fasting state (9 to 14 hour fast) • Total cholesterol (TC), triglycerides (TG), and HDL-C are measured directly • LDL-C is calculated, therefore, TG level should be considered (If TG >400 mg/dL, try to reduce with diet and exercise, or consider direct measurement of LDL-C)

Recommendations

1. A complete fasting lipid profile should be obtained in an individual with other risk factors for coronary disease. [A]
2. Clinical decisions should be based upon lipid profiles done 1 to 8 weeks apart (fasting) with an LDL-C or TC difference of <30 mg/dL. [I]
3. Lipid profiles should not be obtained within 8 weeks of acute hospitalization, surgery, trauma, or infection unless they are obtained within 12 to 24 hours of the event to ensure accuracy. [I]
4. Lipid profiles should not be measured in pregnant women until three to four months post partum. [I]

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	A complete fasting lipid profile should be obtained in individuals with other risk factors for coronary artery disease (CAD)	USPSTF, 2001	I	Good	A
2	Clinical decisions should be based upon lipid profiles done 1 to 8 weeks apart (fasting or no fasting) with an LDL-C or TC difference of less than 30 mg/dL	Working Group Consensus	III	Poor	I
3	Lipid profiles should not be obtained within 8 weeks post-acute hospitalization, surgery, trauma, or infection unless they are obtained within 12 to 24 hours of the event to ensure accuracy	Working Group Consensus	III	Poor	I
4	Lipid profiles should not be measured in pregnant women until three to four months post partum	Working Group Consensus	III	Poor	I

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

G. TG >400 mg/dL, Apply Diet and Exercise to Reduce TG; Consider Direct Measurement of LDL-C

Objective

Identify patients whose LDL-C is confounded by secondary/modifiable causes of hypertriglyceridemia.

Recommendations

1. If TG levels can be brought to <400 mg/dL by dietary or other interventions, then Friedewald's formula can be used to calculate a more exact LDL-C level. [C]
2. If TGs cannot be brought to levels less than 400 mg/dL, then consider measuring LDL-C directly, or estimate the LDL-C using the following equation: [I]

   Estimated LDL-C = (TC – HDL) – 30

3. Screen and treat common causes of elevated TGs: fatty diet, high carbohydrate diets, alcohol use, hypothyroidism, and hyperglycemia. [B]
4. In the absence of secondary causes, the first-line therapy for elevated TGs should be therapeutic life-style changes. [C]

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Use Friedewald's formula to calculate LDL-C – when TG levels can be brought to <400 mg/dL by dietary or other interventions	Friedewald et al., 1972 NCEP ATP-III, 2002	III	Fair	C
2	If TGs are >400 consider directly measuring LDL-C	Friedewald et al., 1972 NCEP ATP-III, 2002 Stone & Blum, 2002	III	Poor	I
3	Screen and treat common causes of elevated TGs	Cleeman, 1998 Friedewald et al., 1972 NCEP ATP-III, 2002 Stone & Blum, 2002	II-3	Fair	B
4	In the absence of secondary causes, the first-line therapy for elevated TGs should be therapeutic life-style changes	Cleeman, 1998 Friedewald et al., 1972 NCEP ATP-III, 2002 Stone & Blum, 2002	II-3	Poor	C

QE = Quality of Evidence R = Strength of Recommendation (see Appendix A in the original guideline document)

H. Is Lipid Profile Abnormal?

Objective

Identify patients who require further evaluation and/or therapy for dyslipidemia.

Classification of Serum Lipids	
Total Cholesterol (TC) mg/dL (mmol/L)	Category
<200 (<5.2) 200 to 239 (5.2 to 6.1) ≥240 (≥ 6.2)	Normal Borderline high High
LDL-Cholesterol mg/dL (mmol/L)	
<100 (<2.6) 100 to 129 (2.6 to 3.3) 130 to 159 (3.4 to 4.0) 160 to 189 (4.1 to 4.8) ≥190 (≥4.9)	Normal Above, near optimal Borderline high High Very high
HDL- Cholesterol mg/dL (mmol/L)	
<40 (<1.0) ≥60 (≥1.6)	Low High
Triglycerides (TG) mg/dL (mmol/L)	
<150 mg/dL (<1.7) 150 to 199 mg/dL (1.7 to 2.2) 200 to 499 mg/dL (2.3 to 5.6) ≥500 mg/dL (≥5.6)	Normal Borderline High High Very High

Recommendation

1. Patients with LDL ≥130 mg/dL, HDL <40 mg/dL, or TG >200 mg/dL should be assessed for further management of dyslipidemia. [C]

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Classify Serum Lipid levels based on degree of elevation of LDL, TG, or low HDL	NCEP ATP-III, 2002	II-2	Good	C

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

I. Encourage Healthy Lifestyle

Objective

Promote lifestyle changes that will decrease the risk of CVD.

Recommendations

1. All adults should be encouraged to adopt healthy lifestyles that may reduce the risk of cardiovascular disease, to include:
    a. Tobacco cessation interventions offered to all smokers [A]

b. Eat a healthy diet [B]
c. Engage in 30 minutes or more of moderate intensity physical activity on most days of the week. [B]

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Advise patients to stop smoking	Fiore et al., 2000 Silagy & Stead, 2001	I	Good	C
2	Provide tobacco cessation interventions to smokers	Fiore et al., 2000	I	Good	A
3	Provide interventions to encourage a healthy diet	Beresford et al., 1997 McCarron et al., 1997	I	Fair	B
4	Encourage 30 minutes or more of moderate intensity aerobic physical activity on most days of the week	Pate et al., 1995 American College of Sports Medicine (ACSM), 1995 Pollock & Wilmore, 1990 Spate-Douglas & Keyser., 1999	I IIa	Fair	B

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

J. Repeat Dyslipidemia Evaluation in 1 to 5 Years

Objective

Provide appropriate clinical follow-up for patients initially at low-risk for CVD.

Recommendations

1. Patients with average or below average risk for atherosclerotic events should be screened for dyslipidemia every five years. [B]

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Patients with average or below average risk for atherosclerotic events should be screened for dyslipidemia every five-year period	NCEP ATP-III, 2002 "A multicenter comparative trial," 1993	III	Fair	B

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

Initiation of Therapy Algorithm

K. Patient with Abnormal Lipid Profile or History of CVD or Diabetes

Patients managed by this guideline algorithm have abnormal lipid profiles (dyslipidemia) or evidence of cardiovascular disease (CVD) or diabetes.

L1. Obtain History, Physical Examination, and Laboratory Tests. Assess for Secondary Causes, Familial Disorders, and Comorbidities

Objective

Detect and if needed treat health disorders that present with an elevated LDL-C or TG, low HDL-C, or metabolic syndrome.

Recommendations

1. Adults with abnormal lipid profiles (dyslipidemia) should be assessed for secondary causes, familial disorders, and other underlying conditions that may influence lipid levels. [I]
2. Assessment for secondary causes should be based on medical history, physical examination and laboratory tests:
    a. Measurement of serum thyroid-stimulating hormone (TSH), blood urea nitrogen (BUN)/creatinine, liver function tests (LFTs), and a dipstick urinalysis should be obtained to exclude hypothyroidism, chronic renal failure, obstructive liver disease, and nephrotic syndrome conditions. [I]
    b. If dipstick urine protein is >1+ (detected in two urine tests), nephrotic syndrome as a secondary cause of elevated LDL-C should be ruled out. [I]
    c. Serum lipids should be assayed six to eight weeks post-TSH normalization to determine the need for additional treatment. [I]
    d. Patients with hypertriglyceridemia should be evaluated for alcohol use, diabetes, and hypothyroidism. Addressing these underlying conditions can improve or normalize triglyceride levels, and failure to address these can render therapy ineffective. [I]
    e. Lipid levels in patients treated for secondary hyperlipidemia should be repeated six to eight weeks post correction of the underlying disorder.
    f. Family members of patients presenting with very severe hypercholesterolemia should be screened to detect other candidates for therapy.
    g. Consider consulting with a specialist to assist the primary care clinician in co-managing patients with familial disorders who do not respond to therapy. [I]

Secondary Causes of Lipid Abnormalities		
Disorder/Patient Characteristic	Effect on Lipids	Laboratory Test for Diagnosis
Chronic renal failure/postrenal transplantation	Increase TG Increase TC Decrease HDL-C	S_{Cr}
DM	Increase TG Increase TC Decrease HDL-C	Glucose, HbA1c
Ethanol use	Increase TG Increase HDL-	--

Secondary Causes of Lipid Abnormalities		
Disorder/Patient Characteristic	Effect on Lipids	Laboratory Test for Diagnosis
	C	
HIV/AIDS Wasting	Increase TG Decrease TC Decrease HDL-C Decrease LDL-C	--
HIV/AIDS (HAART)	Increase TG Increase TC Increase HDL-C	--
Hypothyroidism	Increase TG Increase TC Increase LDL-C	TSH
Inactivity	Decrease HDL-C	--
Nephrotic syndrome	Increase TC Increase LDL-C	Urinalysis, serum albumin
Obesity	Increase TG Decrease HDL-C	--
Obstructive liver disease	Increase TC	LFTs (Alkaline phosphatase, total bilirubin)
Estrogen therapy	Increase TG Decrease LDL Increase HDL	--
Medications	Variable	--

AIDS = acquired immune deficiency syndrome; DM = diabetes mellitus; HAART = highly active antiretroviral therapy; HbA1c = glycosylated hemoglobin; HDL-C = high-density lipoprotein cholesterol; HIV = human immunodeficiency virus; LDL-C = low-density lipoprotein cholesterol; LFTs = liver function tests; SCr = serum creatinine; TC = total cholesterol; TG = triglycerides; TSH = thyroid-stimulating hormone

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Detect and treat secondary cause of dyslipidemia	NCEP ATP-III, 2002 Stone et al., 1997 Stone & Blum, 2002	III	Poor	I
2	Refer familial hypercholesteremia to specialist	Working Group Consensus	III	Poor	I

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

L2. Obtain Baseline Serum Transaminase (ALT/AST) Prior to Starting Lipid Lowering Therapy

Objective

Establish baseline transaminase monitoring parameters prior to initiating lipid lowering therapy.

Recommendations

1. Baseline serum transaminase (alanine aminotransferase [ALT]/aspartate aminotransferase [AST]) should be obtained prior to starting lipid-lowering therapy. [I]
2. Levels of serum transaminase (ALT/AST) should be obtained in patients on statin, 6 to 12 weeks after starting statin therapy, and/or change in dose or combination therapy, then annually or more frequently, if indicated. [I]
3. Levels of serum transaminase (ALT/AST) should be obtained in patients on niacin, 6 to 12 weeks after reaching a daily dose of 1,500 mg and 6 to 12 weeks after reaching the maximum daily dose, then annually or more frequently, if indicated. [I]

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Statins— Evaluate ALT/AST initially, approximately 6 to 12 weeks after starting, then annually or more frequently, if indicated	NCEP ATP-III, 2002	III	Poor	I
2	Nicotinic Acid— Evaluate ALT/AST initially, 6 to 12 weeks after reaching a daily dose of 1,500 mg, 6 to 12 weeks after reaching the maximum daily dose, then annually or more frequently, if indicated	NCEP ATP-III, 2002	III	Poor	I

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

M1. History of Acute Coronary Syndrome in Past 6 Months?

Objective

Identify patients with recent acute coronary syndrome (ACS) for whom there is a compelling need for statin therapy regardless of current lipid levels.

Recommendations

1. A lipid panel should be drawn at the time of admission for all patients with suspected acute coronary syndrome (ACS). [C]
2. Initiating a moderate- to high-dose statin therapy prior to hospital discharge may be considered in patients admitted with ACS irrespective of their lipid profile. [B]
3. Patients with recent ACS (within the past 6 months) should be on a moderate dose of statin therapy to reduce LDL-C level below 100 mg/dL. [A]
4. A lower target (70 mg/dL) may be considered for very high-risk patients. [B]

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	For patients admitted with ACS, a lipid panel should be drawn at the time of admission	Working Group Consensus	III	Poor	I
2	Patients should be started on moderate- to high-dose statins prior to hospital discharge and irrespective of their lipid profile	Bybee et al., 2002 Lorenz et al., 2005 Stenestrand & Wallentin, 2001	I	Good	B
3	If not started on a statin prior to hospital discharge, then one should be started within 6 months post-ACS	de Lemos et al., 2004 Cannon et al., 2004	I	Good	A
4	An optional lower target for LDL-C may be considered for post-ACS patients	Cannon et al., 2004	I	Good	B

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

M2. History of CVD or DM and LDL-C Above Goal?

(See Screening Algorithm, Annotations B and C)

M3. Calculate 10-Year Risk Score for CVD

Objective

Determine short-term risk (i.e., over ten years) as the basis for determining the type and intensity of interventions.

Recommendations

1. A global 10-year risk for CVD should be calculated to assess the short-term (10-year) absolute risk of a CVD event. [A]
2. The Framingham Risk Calculator should be used, as it is the most commonly used and readily available calculator validated in numerous populations. [I]
   http://hin.nhlbi.nih.gov/atpiii/calculator.asp?usertype=prof

3. Other risk markers or measure of atherosclerotic burden may be useful to adjust the risk category, if they have been validated to have independent prognostic value. [C]

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	A global 10-year risk for CVD should be calculated to assess the short-term (10 years) absolute risk of a CVD event	Grover, Coupal, & Hu, 1995 Grover et al., 2000 Grundy et al., 2004	I	Good	A
2	The Framingham Risk Calculator is the most commonly used and readily available calculator validated in numerous populations	Grundy et al., 1999 Sheridan, Pignone, & Mulrow, 2003 Wilson et al., 1998	III	Poor	I
3	Other risk markers or measures of atherosclerotic burden may be useful to adjust the risk category	Ford et al., 1998 Greenland et al., 2000; 2004 O'Donnel, 2004 Pearson et al., 2003 Pletcher et al., 2004 Ridker, 2001	III	Fair	C

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

N. Determine Risk for CVD and Establish the Goal for Interventions

Recommendations

1. Goals of lipid lowering therapy should be tailored to risk level and based upon the balance between benefits, risks, and patient preferences. [C]

Goals of Therapy for Secondary Prevention

2. LDL-C should be lowered to <100 mg/dL for patients with a recent ACS. [A]
3. An optional lower target for LDL-C (<70 mg/dL) may be considered for very high-risk post-ACS patients. [B]
4. LDL-C should be lowered to <100 mg/dL for patients with previous documented CHD or CVD equivalent (DM with other major risk factors) for secondary prevention. [A]
5. LDL-C should be lowered to <130 mg/dL for patients with DM without other major risk factors for secondary prevention. [C]

Goals of Therapy for Primary Prevention

6. LDL-C should be lowered to <100 mg/dL for patients with high 10-year risk >20 percent. [B]
7. LDL-C should be lowered to <130 mg/dL for patients with intermediate 10-year risk (15 to 20 percent). [B]

8. LDL-C should be lowered to <130 mg/dL for patients with intermediate 10-year risk (10 to 14 percent). [C]
9. LDL-C should be lowered to <160 mg/dL for patients with low 10-year risk. [I]
10. LDL-C reduction of 30 to 40 percent from baseline may be considered an alternative therapeutic strategy for patients who cannot meet the above goal.

Table. Goals of Lipid Lowering Therapy

	Risk Category	Number of Risk Factors (RF)	10-Year Risk	LDL-C Goal mg/dL *	Remarks
1	Recent ACS	N/A	N/A	<100	Option <70 mg/dL
2	CHD or equivalent (DM with other risk factors)	N/A	N/A	<100	Optional <130 for DM with no other risk factors
3	High	2 + RF	≥20%	<100	--
4	Intermediate	2 +RF	15 to 20%	<130	--
5			10 to 14% **	<130	--
6	Low	0-1 RF	N/A	<160	--

N/A = Not applicable
* Recommendations are based on quality of evidence for improving CVD outcomes.
** There is insufficient evidence at this time to recommend routine screening for other risk markers not included in the risk index (e.g., FH, high sensitive C-reactive protein [hsCRP], metabolic syndrome, depression), or evidence of significant atherosclerotic burden (e.g., high coronary artery calcification scores, intima medial thickness, abnormal brachial reactivity, or abnormal ankle-brachial index). These risk markers have independent prognostic value whereby abnormal values can shift risk percent upward across treatment thresholds with more robust evidence for efficacy. Therefore, they may be useful in the intermediate risk patient for whom it is less convincing that drug therapy would have a meaningful impact on outcomes. Example: Patient with a 10-year risk of 13 percent in whom an abnormal test with a proven adjusted relative risk of >2 would shift the patient to a high-risk category (across a 20 percent, 10-year risk threshold).

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Target lipid lowering therapy to risk	"27th Bethesda Conference," 1996 Grundy et al., 2004	I	Good	C
	Secondary Prevention				
2	Goal <100 mg/dL for recent ACS patients	Schwartz et al., 2001 Cannon et al., 2004 Nissen et al., 2004	I	Good	A

	Recommendation	Sources of Evidence	QE	Overall Quality	R
3	An optional lower target for LDL-C may be considered for severe post-ACS patients	Cannon et al., 2004	I	Good	B
4	Goal <100 mg/dL for patients with previous documented CHD or CVD or CVD equivalent = DM	Sacks et al., 1996 Heart Protection Study Collaborative Group, 2002 LaRosa, He, & Vupputuri, 2005	I	Good	A
5	Goal <130 mg/dL for patients with DM without other major risk factors	Haffner et al., 1998 NCEP Consensus	III	Poor	C
	Primary Prevention				
6	Goal <100 mg/dL for high-risk group	Sever et al., 2003 Heart Protection Study Collaborative Group, 2002 "Screening experience and baseline characteristic in the West of Scotland Coronary Prevention Study," 1995	I	Fair	B
7	Goal <130 mg/dL for patients with intermediate 10-year risk (15 to 20%)	Downs et al., 1998	I	Fair	B
8	Goal <130 mg/dL for intermediate-risk group 10 to 14%	NCEP ATP-III, 2002	III	Poor	C
9	Goal <160 mg/dL for low-risk group	Consensus Group	III	Poor	I

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

O. Initiate Lipid Lowering Therapy to Achieve Goal

Objective

Select an appropriate therapy based on LDL-C baseline level and other risk factors for CVD.

Recommendations

Non-Pharmacologic Therapy

1. Therapeutic lifestyle changes (TLC) should be recommended for ALL patients with dyslipidemia, regardless of risk or baseline LDL-C level. [C]

Drug Therapy for Secondary Prevention

2. All patients with a recent ACS should be on at least a moderate dose of statin therapy. [A]
3. Statin drug therapy should be initiated for patients with previous documented CHD or CVD equivalent (diabetes with other major risk factors) if baseline LDL-C is ≥100 mg/dL. [A]
4. Statin drug therapy should be initiated for patients with documented DM with no major risk factors if baseline LDL-C is ≥130 mg/dL. [C]
5. Statin drug therapy may be considered optional for all patients with CHD or CVD equivalent (diabetes with other major risk factors) regardless of LDL-C baseline. [B]

Drug Therapy for Primary Prevention

6. Drug therapy should be initiated for high-risk patients (>20%) if baseline LDL is ≥130 mg/dL. [B]
7. Drug therapy is optional to consider in high-risk patients (>20%) if baseline LDL is 100 to 129 mg/dL. [B]
8. Drug therapy may be offered to patients with high-intermediate risk (15 to 20 percent) if baseline LDL is ≥130 mg/dL. [B]
9. Drug therapy may be offered to patients with low-intermediate risk (10 to 14 percent) if baseline LDL is ≥160 mg/dL. [C]
10. Drug therapy may be offered to low-risk patients (<10 percent) if baseline LDL is ≥190 mg/dL. [I]

The following table summarizes the lipid lowering strategy for patients in primary prevention. Individual management of cardiovascular risk should be informed mainly by the probable absolute magnitude of treatment benefits. Lowering absolute risk involves modification of multiple risk factors/co-morbidities, not only LDL-C levels. Therefore, these goals should serve as a general guide and clinical judgment should be used to modify the goals as appropriate for each patient.

Table. Dyslipidemia Therapy Thresholds and Goals

	Risk Category	Disease Status or Risk Factors	Calculated 10-Year Risk	TLC	LDL-C Level for Considering Statin Drug Therapy	LDL Goal of Therapy
Secondary Prevention	Very high	Recent ACS	N/A	All	All	<100 mg/dL <70 optional
		CHD or DM with other risk factors	N/A	All	≥100 mg/dL	<100 mg/dL
		DM with no other risk factors	N/A	All	≥130 mg/dL 100 to 129 optional	<130 mg/dL

	Risk Category	Disease Status or Risk Factors	Calculated 10-Year Risk	TLC	LDL-C Level for Considering Statin Drug Therapy	LDL Goal of Therapy
Primary Prevention	High	More than 2 RF	≥20%	All	≥130 (or HDL <40) 100 to 129 optional	<100 mg/dL
	Intermediate	More than 2 RF	15 to 20%	All	≥130 mg/dL	<130 mg/dL
			10 to 14% *	All	≥160 mg/dL	<130 mg/dL
	Low	0 or 1 RF	N/A	All	≥190 mg/dL	<160 mg/dL

LDL-C reduction of 30-40 percent from baseline may be considered an alternative therapeutic strategy for patients who cannot meet the above goals.

N/A = Not applicable; TLC = Therapeutic Lifestyle Changes; RF = Risk Factor
* There is insufficient evidence at this time to recommend routine screening for other risk markers not included in the risk index (e.g., FH, hsCRP, metabolic syndrome, depression), or evidence of significant atherosclerotic burden (e.g., high coronary artery calcification scores, intima medial thickness, abnormal brachial reactivity, or abnormal ankle-brachial index). These risk markers may be useful in the intermediate risk patient for whom it is less convincing that drug therapy would have a meaningful impact on outcomes.

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Therapeutic lifestyle changes should be recommended for ALL patients	NCEP ATP-III, 2002	III	Fair	C
2	For recent ACS patients, moderate to high-dose statins should be given prior to hospital discharge; If not started prior to discharge, then statin therapy should be started within 6 months post ACS	de Lemos et al., 2004 Schwartz et al., 2001 Cannon et al., 2004	I	Good	A
3	Initiate drug therapy in all patients with previous documented CHD or CVD equivalent (DM with other major risk factors) if baseline LDL-C is ≥100 mg/dL	Sacks et al., 1996 "Randomised trial," 1994 Heart Protection Study Collaborative Group 2002 "Prevention of cardiovascular events," 1998 Shepherd et al., 2002 LaRosa, He, & Vupputuri, 2005	I	Good	A

	Recommendation	Sources of Evidence	QE	Overall Quality	R
4	Drug therapy should be initiated for patients with DM and NO major risk factors) if baseline LDL-C is ≥130 mg/dL	NCEP Consensus of Experts	III	Poor	C
5	Drug therapy may be considered for all patients with DM and other risk factors regardless of LDL baseline	Colhoun et al., 2004 LaRosa, He, & Vupputuri, 2005	I	Fair	B
6	Drug therapy should be initiated for high-risk patients (10-year risk >20%) if baseline LDL is ≥130 mg/dL	Downs et al., 1998 Sever et al., 2003 "Screening experience and baseline characteristics in the West of Scotland Coronary Prevention Study", 1995	I	Good	A
7	Consider drug therapy in high-risk patients if baseline LDL is 100 to 129 mg/dL	Heart Protection Study Collaborative Group, 2002	I	Fair	B
8	Offer drug therapy for high- and intermediate-risk (15 to 20%) if baseline LDL is ≥130 mg/dL	Sever et al., 2003 Downs et al., 1998 "Screening experience and baseline characteristics in the West of Scotland Coronary Prevention Study," 1995	I	Fair	B
9	Offer drug therapy for low-intermediate risk (10-15%) patients if baseline LDL is ≥160	NCEP ATP-III, 2002	III	Poor	C
10	Offer drug therapy for low-risk patients (<10%) if baseline LDL is ≥190 mg/dL	NCEP ATP-III, 2002	III	Poor	I

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

P. Therapeutic Lifestyle Change (TLC)

For secondary prevention of recurrent CVD events, non-pharmacologic therapy is always indicated, but should not delay appropriate pharmacotherapy.

For primary prevention of CVD, emphasis on TLC is an important component and is effective in reducing CVD risk by lowering LDL-C and blood pressure. Ample time should be given (3 to 6 months) for patients to improve their LDL-C and total lipid profile prior to starting lipid-lowering medication. Patients failing primary clinician efforts may benefit from medical nutrition therapy (MNT) provided by a registered dietician or other qualified nutritionist (see Appendix C, Medical Nutrition Therapy in the original guideline document).

TLC is provided in a step-wise approach focused on initiating TLC components and followed by subsequent evaluation of the effect on LDL-C and moving to intensify MNT as indicated. See Figure 2 "Step Wise Care Approach" in the original guideline document.

P1. Medical Nutrition Therapy

Objective

Improve dyslipidemia using medical nutrition therapy (MNT).

Recommendations

1. Diet intervention should be the first step in lipid lowering therapy. [B]
2. Patients whose initial treatment is TLC should be given 3 to 6 months of dietary therapy prior to beginning medication and longer, if lipids are improving and nearing LDL thresholds. [B]
3. Initial diet should focus on reduction of saturated fats to <7 percent of total calories and dietary cholesterol to <200 mg/day similar in composition to the TLC diet (formerly Step II diet). [B]
    a. The range of 25 to 35 percent of total calories from fat is to be paired with keeping saturated fats and trans-fatty acid percents of total calories low.
    b. Advise 10 percent monounsaturated fat, <7 percent saturated fat, <200 mg cholesterol diet.
    c. If TGs are elevated, ensure that blood glucose is under control, limit alcohol and simple sugars, and evaluate need for weight loss. Emphasis should be placed on weight reduction and physical activity.
    d. Limit foods with trans fatty acids (e.g., stick margarine, shortening, and commercially baked products and processed food).
    e. Select >5 to 6 servings/day fruits and vegetables and six servings/day whole-grain products.

4. Patient's specific diet should be individualized based on nutrition assessment, other CVD risk factors, other disease conditions, and patient's lifestyle. [I]
5. Patients should be evaluated 4 to 6 weeks after their initial consultation. A lipid profile and anthropometric data should be analyzed. Further dietary intervention may include:
    a. Increase soluble (viscous) fiber to 10 to 25 g/day to lower LDL-C. [B]
    b. Increase plant sterols/stanols to 2 g/day to lower LDL-C. [B]
    c. Include nuts such as walnuts and almonds (1 oz. ~5 times/week) and soy protein (25 g/day or 8 oz. of tofu) to lower LDL-C. [B]
    d. Select fatty fish (average of 7 oz./week) (fish oil) to lower TG. [B]

6. Weight management for overweight and obese patients should be encouraged to lower LDL-C and TG and to reduce CV risk. [B]
7. Patients in whom triglycerides >500 mg/dL should receive strict diet therapy including avoidance of alcohol, restriction of dietary fat, and avoidance of concentrated carbohydrates (sweets). For triglycerides >1000 mg/dL a very low fat diet should be instituted quickly to reduce chylomicronemia and risk of acute pancreatitis.

8. Patients with evidence of metabolic syndrome should receive MNT that incorporates the additional protocol for weight management with increased physical activity. [B]

Table. Essential Components of Therapeutic Lifestyle Changes (TLC)	
Component	Recommendation
LDL-raising nutrients Saturated fats*	Less than 7% of total calories
Dietary cholesterol	Less than 200 mg/day
Therapeutic options for LDL lowering	
Plant stanols/sterols	2 grams per day
Increased viscous (soluble) fiber	10 to 25 grams per day
Total calories (energy)	Adjust total caloric intake to maintain desirable body weight/prevent weight gain
Physical activity	Include enough moderate exercise to expend at least 200 kcal per day
*Trans fatty acids are another LDL-raising fat that should be kept at a low intake.	

Table. Macronutrient Recommendations for the TLC Diet	
Component	Recommendation
Polyunsaturated fat	Up to 10% of total calories
Monounsaturated fat	Up to 20% of total calories
Total fat	25 to 35% of total calories*
Carbohydrate**	50 to 60% of total calories*
Dietary fiber	20 to 30 grams per day
Protein	Approximately 15% of total calories
*ATP-III allows an increase of total fat to 35 percent of total calories and a reduction in carbohydrates to 50 percent for persons with the metabolic syndrome. Any increase in fat intake should be in the form of either polyunsaturated or monounsaturated fat. *Carbohydrate should derive predominantly from foods rich in complex carbohydrates including grains—especially whole grains—fruits, and vegetables.	

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Use MNT for lowering LDL-C.	Delahanty et al., 2001; 2002 Sikand et al., 2000 Yu-Poth et al., 1999	I	Good	B
2	Recommend 3 to 6 months of diet therapy prior to pharmacotherapy, if needed	NCEP ATP-III, 2002	I	Fair	B
3	Recommend a low saturated fat, low cholesterol diet	NCEP ATP-III, 2002	II	Good	B
4	Reduce saturated fats to less	Hooper et al., 2001	I	Fair	B

	Recommendation	Sources of Evidence	QE	Overall Quality	R
	than 7% of total calories	Krauss et al., 2000 Lichtenstein et al., 2002 NCEP, 2001			
5	Provide individualized dietary counseling with reinforcement during follow-up	NCEP ATP-III, 2002 Tang et al., 1998	I	Fair	B
6	Consume viscous fiber (at least 10-25 grams/day)	Brown et al., 1999 Kris-Etherton et al., "High-soluble fiber food," 2002	I	Fair	B
	Eat plant sterols/stanol esters (2 to 3 g/day)	Christiansen et al., 2001 Jenkins et al., 2003; 2005 Lichtenstein & Deckelbaum, 2001 Maki et al., 2001	I	Fair	B
	Eat 5 ounces of nuts per week	Jenkins et al., 2003 Krauss et al., 2000 Lovejoy et al., 2002 Sabate, 2003	I	Fair	B
	Eat 25 grams/day of soy protein	Anderson, Johnstone, & Cook-Newell, 1995 Erdman, 2000 Merritt, 2004 Meyer et al., 2004	I	Fair	B
	Eat at least two servings of fish per week	Kris-Etherton, "Fish consumption," 2002 NCEP ATP-III, 2002	I	Fair	B
7	Reduce caloric intake and increase physical activity to maintain desirable body weight	Krauss et al., 2000 NCEP ATP-III, 2002	I	Fair	B
8	Low fat diet for TGs >500 mg/dL; Very low fat diet if TGs >1000 mg/dL	American Dietetic Association (ADA), 2001 NCEP ATP-III, 2002	I	Fair	B
9	Recommend MNT for management of metabolic syndrome	ADA, 2001 NCEP ATP-III, 2002 Nieman et al., 2002 Sartorio et al., 2003	I	Fair	B

QE = Quality of Evidence; Strength of Recommendation (see Appendix A in the original guideline document)

P2. Physical Activity/Exercise and Weight Control

Recommendations

1. Moderate intensity levels of physical activity should be performed for at least 30 minutes most, preferably all, days of the week. [B]
2. In patients with CVD, aerobic exercise should not precipitate angina.

3. Increased physical activity through lifestyle change should be encouraged, as it is equally as effective as structured exercise in reducing body fat, improving cardiorespiratory fitness, and improving cardiovascular risk factors. [B]
4. Physical activity, through lifestyle change or structured exercise, should be encouraged to maintain weight control (or weight loss if overweight or obese), to improve insulin resistance, and increase HDL-C. [B]

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Increase physical activity to improve lipid profile	Fahlman et al., 2002 Halbert et al., 1999 Kraus et al., 2002 Stefanick et al., 1998	I	Fair	B
2	Engage in moderate levels of exercise/physical activity for at least 30 minutes, on most days of the week	ACSM 2002 Pate et al., 1995 U.S. DHHS, 1996	I	Fair	B
3	Increased physical activity is just as effective as structured exercise in reducing body fat, improving cardiorespiratory fitness	Lee et al., 2001 Manson et al., 1999; 2002 Wannamethee, Shaper, & Walker, 2000	II	Fair	B
4	Exercise should be encouraged to maintain weight control (or weight loss if overweight or obese)	National Heart Lung, and Blood Institute (NHLBI), 1998 Scranton et al., 2004	II	Fair	B

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

Q1. Pharmacotherapy: Monotherapy

Objective

Reduce the risk of CVD events and achieve lipid goals through the use of optimal pharmacotherapy.

Recommendations

1. Pharmacologic treatment of dyslipidemia should be individualized and dictated by lipid levels. [B]

Elevated LDL-C

2. Statins are first line agents in primary and secondary prevention of CVD regardless of HDL-C or TG level. [A]
3. Moderate doses of formulary statins (to achieve an LDL-C reduction of 25 percent or greater) should be initiated unless a patient is considered to be at greater than usual risk for adverse events from statins (e.g., myopathy). [A]
4. For patients who cannot tolerate statins, niacin or resins should be considered for treatment. [A]

5. There is insufficient clinical outcome evidence to recommend ezetimibe monotherapy for reduction of CV risk. [I]
6. Ezetimibe can be considered for lowering LDL-C in patients who are unable to tolerate other lipid-lowering drugs. [A]
7. The dose of statin should be adjusted at 6 to 12 week intervals until individual LDL-C goals are achieved or statin doses have been maximized. [I]

Isolated Hypertriglyceridemia

8. Niacin, fibrates, or fish oil supplements may be used in treatment of hypertriglyceridemia. [B]

Isolated Low HDL-C

9. For secondary prevention, gemfibrozil or niacin may be used in patients with isolated low HDL-C and normal LDL-C. [A-Gemfibrozil; B-Niacin]

Safety and Follow-Up

10. Patients treated with statins or fibrates should be educated regarding the importance of recognizing and reporting any unexplained muscle tenderness, pain, or weakness. [I]
11. Lipid profiles should be repeated 6-12 weeks after initiation of therapy and/or change in dose and/or combination therapy. [B]
12. Liver function tests (LFTs) should be performed prior to and after 12 weeks following initiation of treatment, any elevation in dose, and periodically thereafter in those receiving statins, fibrates, or niacin. [I]
13. Creatine kinase (CK) levels should be obtained in patients who develop muscle pain, weakness, or tenderness after institution of statin or fibrate therapy. [I]

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Pharmacologic treatment of dyslipidemia should be individualized and is dictated by lipid levels	NCEP ATP-III, 2002	I	Fair	B
2	Statins are first line agents in primary and secondary prevention regardless of baseline TG or HDL-C level	Primary Prevention: Downs et al, 1998 Sever et al., 2003 Colhoun et al., 2004 "Screening experience and baseline characteristics in the West of Scotland Coronary Prevention Study," 1995 Secondary Prevention: Sacks et al., 1996 4S, 1994 Heart Protection Study Collaborative Group, 2002	I	Good	A

	Recommendation	Sources of Evidence	QE	Overall Quality	R
		"Prevention of cardiovascular events," 1998 Shepherd et al., 2002			
3	Moderate doses of formulary statins (to achieve an LDL-C reduction of 25% or greater) should be initiated (unless greater than usual risk for adverse events)	Primary Prevention: Downs et al., 1998 "Screening experience and baseline characteristics in the West of Scotland Coronary Prevention Study," 1995 Secondary Prevention: Sacks et al., 1996 4S, 1994 Heart Protection Study Collaborative Group, 2002 "Prevention of cardiovascular events," 1998 Serruys et al., 2002 Shepherd et al., 2002 Cannon et al., 2004	I	Good	A
4	Consider treatment with other lipid lowering agents (niacin or resins) for patients who cannot tolerate statins	Primary Prevention: Frick et al., 1993 Lipid Research Clinics Program–Coronary Primary Prevention Trial (LRC-CPPT), 1984 Secondary Prevention: "Clofibrate and niacin in coronary heart disease," 1975 Jamshidi et al., 2002 Robins, Collins, & Rubins, 1999	I	Good	A
5	Use of ezetimibe monotherapy for preventing CVD	Working Group Consensus	III	Poor	I
6	Ezetimibe can be considered for lowering LDL-C in patients who are unable to tolerate other lipid-lowering drugs	Bays et al., 2001 Knopp et al., "Evaluation of the efficacy," 2003 Knopp et al., "Effects of ezetimibe," 2003 Sudhop et al., 2002	I	Good	A
7	Aggressive early treatment with a moderate dose of statins for all patients with recent ACS	Cannon et al., 2004 Nissen et al., 2004	I	Good	A
8	Dose of statin should be adjusted at 6 to 12 week intervals until individual LDL-C goals are achieved or statin doses have been maximized	Working Group Consensus	III	Poor	I
Isolated Hypertriglyceridemia					

	Recommendation	Sources of Evidence	QE	Overall Quality	R
9	Consider niacin, fibrates, or fish oil supplements to lower TGs	Niacin NCEP ATP-III, 2002 Fibrates NCEP ATP-III, 2002 Fish Oils Harris 1997 Farmer et al., 2001	I	Fair	B
		Isolated Low HDL-C			
10	Gemfibrozil	Robins, Collins, & Rubins, 1999	I	Good	A
11	Niacin to increase HDL-C	King et al., 1994 Lavie, Mailander, & Milani, 1992 Miller et al.,1993; 1995 Vega & Grundy, 1989	I	Fair	B
		Safety and Follow-Up			
12	Provide patients with education about unexplained muscle tenderness, pain, or weakness	NCEP ATP-III, 2002	III	Poor	I
13	Repeat lipid profile in 6-12 weeks after initiation of therapy and/or change in dose and/or with combination therapy	Benner et al., 2004 NCEP ATP-III, 2002	II	Fair	B
14	LFT should be performed prior to and after 6-12 weeks following initiation/change of dose, and periodically thereafter in those receiving statins, fibrates, or niacin	NCEP ATP-III, 2002	III	Poor	I
15	Obtain CK levels in patients who develop muscle pain, weakness, or tenderness after institution of statin or fibrate therapy	NCEP ATP-III, 2002	III	Poor	I

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

Q2. Pharmacotherapy: Combination Therapy

Objective

Achieve lipid goals through the use of combination pharmacologic agents.

Recommendations

LDL-C Lowering Combination Therapy [ONLY FOR SECONDARY PREVENTION]

1. For patients not at goal, monotherapy should be titrated until goal is achieved or maximum tolerable dose has been reached. [C]
2. Combination therapy to achieve LDL-C goal may be considered for carefully selected patients who do not achieve the LDL-C goal with maximally tolerated monotherapy. [I]
3. Combination lipid-lowering therapy should include a statin unless the patient is unable to tolerate statins. [A]
4. Addition of a resin to the statin can be considered for secondary prevention in patients not meeting their LDL-C goals on maximally tolerated doses of statins. [B]
5. Addition of niacin or a resin to the statin can be considered in patients not meeting their LDL-C goals to further reduce the LDL-C level. [B]
6. Addition of ezetimibe to the statin can be considered in patients not meeting their LDL-C goals on maximally tolerated doses of statins and unable to tolerate niacin or a resin to reduce the LCL-C level. [I]
7. In patients unable to tolerate statins and not achieving their LDL-C goals with niacin or resins, a combination of both resin and niacin may be considered. [B]
8. In any combination therapy the lowest possible dose of statin should be used to achieve lipid goals. When combined with fibrates (greatest risk), niacin, or possibly ezetimibe, the risk of adverse events with statins (e.g., muscle toxicity) appears to increase with increasing statin doses. [C]

Elevated LDL-C and Very High Triglycerides (>500 mg/dL)

If non-HDL goals cannot be achieved with a statin (or other LDL-lowering regimen) alone, a TG-lowering drug may be added to the statin. Choices are niacin, a fibrate, and fish oils.

9. Combination therapy with statins and niacin, fish oils, or fibrates can be considered for the secondary prevention of CVD in patients with elevated LDL-C and very high TGs. [C]
10. Combination therapy with niacin and fibrates can be considered for the secondary prevention of CVD in patients with elevated LDL-C and very high TGs in patients unable to tolerate statins. [C]

Very High Triglycerides and/or Low HDL-C Without Elevated LDL-C

11. For secondary prevention of CVD in patients with either low HDL-C or very high triglycerides and no elevation of LDL-C levels, combination therapy with statin plus niacin, fibrate, or fish oil may be considered. [C]
12. Combination therapy with niacin and fibrates and/or fish oils can be considered in patients unable to tolerate statins. [C]

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Combination lipid-lowering therapy should include a	Colhoun et al., 2004 Heart Protection Study	I	Substantial	A

	Recommendation	Sources of Evidence	QE	Overall Quality	R
	statin unless the patient is unable to tolerate statins	Collaborative Group, 2004			
2	In combination therapy with a statin, the lowest possible dose of statin should be used to achieve lipid goals and minimize complications	Work Group Consensus	III	Poor	C
3	Combination therapy should be reserved for patients on secondary prevention	Work Group Consensus	III	Poor	I
4	Addition of niacin to the statin can be considered in patients on secondary prevention not meeting their LDL-C goals on maximally tolerated doses of statins	Zhou et al., 2004	I	Good	B
5	Addition of a resin to the statin can be considered in patients not meeting their LDL-C goals on maximally tolerated doses of statins	Brown et al., 1990	I	Good	B
6	Addition of ezetimibe to the statin can be considered for lowering LDL-C levels in patients not meeting their LDL-C goals on maximally tolerated doses of statins and unable to tolerate niacin or a resin	Gagne et al., 2002	I	Good	I
7	Combination of resin and niacin can be considered in patients unable to tolerate statins and not achieving their LDL-C goals with niacin or resins alone	Blankenhorn et al., 1987 Brown et al, 1990	II	Good	B
8	Combination of statins and niacin, fish oils, or fibrates can be considered in patients with elevated LDL-C and very high TGs	Working Group Consensus based upon clinical reasoning	III	Poor	C
9	Combination of niacin and fibrates can be considered in patients with elevated LDL-C and very high TGs who are unable to tolerate statins	Working Group Consensus based upon clinical reasoning	III	Poor	C
10	Combination of statin and niacin, fibrate, or fish oil may be considered in patients who have achieved their	Working Group Consensus based upon clinical reasoning	III	Poor	C

	Recommendation	Sources of Evidence	QE	Overall Quality	R
	LDL-C goal or are without elevated LDL-C, and have either low HDL-C or very high TGs				
11	Combination of niacin and fibrates and/or fish oils can be considered in patients with elevated LDL-C very high TGs who are unable to tolerate statins	Working Group Consensus based upon clinical reasoning	III	Poor	C

QE = Quality of Evidence; OQ = Overall Quality; SR = Strength of Recommendation (see Appendix A in the original guideline document)

R. Repeat Dyslipidemia Evaluation in 1 to 2 Years (Patients NOT on Therapy)

Objective

Provide appropriate clinical follow-up for patients not on therapy.

Recommendation

1. If the initial dyslipidemia screening reveals TC >200 mg/dL, or fasting LDL-C >130 mg/dL or HDL-C <40 mg/dL, but LDL-C level is under the recommended goal level based upon CV risk, the patient will be at low-risk for lipid-related events over a one to two-year period and thus, should be reevaluated for dyslipidemia in one to two years.

Follow-up of Therapy Algorithm

S. Address Adherence to Therapy

Objective

Identify causes of inadequate response to therapy following dose or stepwise titration.

Recommendations

1. Adherence to therapy should be assessed at every visit, through history, pill count, and/or administrative records especially if therapeutic goals have not been reached [I]
2. Adherence to lipid-lowering medication regimens may be improved by a multi-pronged approach [I] including:
    a. Evaluation of medication side effects
    b. Simplifying medication regimens to incorporate patient preference

c. Addressing barriers for obtaining the medications (administrative, economic, etc.)
d. Coordination with other healthcare team members to improve monitoring of adherence with prescriptions of pharmacological and lifestyle modification
e. Patient and family education about their disease/treatment regimens
f. Evaluation for depression

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Assess medication adherence at each visit through history, pill count, or medical record review	Working Group Consensus	III	Poor	I
2	Consider a multi-pronged approach to improve adherence to medication regimens	Working Group Consensus	III	Poor	I

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

T. Does The Patient Have Elevated TG Level, or Low HDL-C Level, or Metabolic Syndrome?

The goal of dyslipidemia management is ultimately to decrease CV risk, and the evidence is best at reducing such risk through LDL-C lowering therapies. LDL-C remains the treatment priority, and should be addressed regardless of the TG level. Once the LDL-C goal has been reached, treatment attention may shift to obtain optimal lipoprotein profiles.

U. Evaluation and Treatment of High Triglycerides

Objective

Evaluate and treat TG levels above 200 mg/dL.

Treatment for Hypertriglyceridemia		
TG >200 to 499 mg/dL	TG $\geq$500 mg/dL	TG >1000 mg/dL
• Lifestyle management • Weight loss • Alcohol cessation • Secondary causes	• Very low fat diet • Low concentrated carbohydrate diet • Alcohol cessation • Secondary causes • Consider	• Strict MNT (avoidance of alcohol, fat, and restrict calories) • Secondary causes • Drug therapy, if no response to above • Consider

Treatment for Hypertriglyceridemia		
TG >200 to 499 mg/dL	TG ≥500 mg/dL	TG >1000 mg/dL
	drugs, if no response to above • Consider referral	referral

Recommendations

1. Patients with elevated TG (≥200 mg/dL) should have a repeat fasting lipid profile and, if persistent, receive intensive MNT, an appropriate exercise program, and be screened for underlying causes. [B]
2. Drug therapy may be considered in patients with very high TG levels (≥ 500 mg/dL) that do not respond to lifestyle interventions and the treatment of underlying causes of elevated TG, for the purpose of preventing pancreatitis. [I]
3. Effective drugs for lowering hypertriglyceridemia include fibrates, niacin, and fish oil. [B]

Table. Drug Treatment for Hypertriglyceridemia

TG 500 to 1000 mg/dL		
	Drug	Efficacy (Expected % Reduction in TG)
Initial	Fibrates	-20 to -50
Alternate	Niacin	-20 to -35
	n-3 PUFA Supplements, Omega-3 Fatty Acids/Fish Oils	-20 to -30

- Fibrates are contraindicated in severe renal disease.
- Niacin is contraindicated in hepatic disease and relatively contraindicated in DM, gout, and history of complicated/active peptic ulcer disease (PUD).

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Elevated TG should receive intensive MNT, exercise, and screening for underlying causes	NCEP ATP-III, 2002 Stone & Blum, 2002	II-3	Fair	B
2	Consider drug therapy to prevent pancreatitis	Cleeman, 1998 NCEP ATP-III, 2002 Stone & Blum, 2002	III	Poor	I
3	Use of fibrates, niacin, and fish oil to lower hypertriglyceridemia	Farmer et al., 2001 Harris, 1997	I	Fair	B

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

V. Evaluation and Treatment of Low HDL-C

Objective

Reduce risk of CVD through raising the level of HDL-C.

Recommendations

1. Patients with CVD who have low HDL-C (<40 mg/dL), TG >200 mg/dL, and normal levels of LDL-C may benefit from gemfibrozil therapy. [A]
2. Lifestyle modifications, including weight loss, exercise, and smoking cessation should be given high priority in the therapeutic plan for patients with low HDL-C. [B]
3. CVD patients with low HDL-C (<40 mg/dL) may be considered for treatment with niacin. [B]

Table. Drug Treatment for Isolated Low HDL-C

LDL-C <130 and Low HDL-C		
Drug	Efficacy (Expected % Reduction in TG)	
Gemfibrozil	LDL-C +10 to –35	HDL-C +2 to 34

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	CVD patients with HDL-C <40 mg/dL, triglycerides >200 mg/dL, benefit from gemfibrozil therapy	Robins, Collin, & Rubins, 1999	I	Good	A
2	Lifestyle modifications, including weight reduction, smoking cessation, and exercise improve HDL-C level. Aerobic exercise Weight loss	Dattilo & Kris-Etherton, 1992 Haskell et al., 1988 Kokkinos et al., 1995 Superko & Haskell, 1987 Wood et al., 1991	II	Fair	B
3	CVD patients with low HDL-C, may benefit from niacin	King et al., 1994 Lavie et al., 1992 Miller et al., 1993; 1995 Vega & Grundy, 1989	I	Fair	B

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

W. Evaluation and Treatment of Metabolic Syndrome

Objective

Identify therapeutic treatment options for individuals with metabolic syndrome.

Recommendations

1. TLC should be initiated for patients diagnosed with metabolic syndrome. [B]
2. Lifestyle modification for weight reduction through diet and increased physical activity is indicated for patients diagnosed with metabolic syndrome. [B]
3. Drug therapy to alter insulin resistance or low HDL-C or elevated TG has not been demonstrated to improve CVD outcomes in patients with metabolic syndrome and as such, clinicians will have to individualize therapy. [I]

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	TLC should be initiated for patient in which metabolic syndrome is indicated	NCEP ATP-III, 2002	III	Fair	B
2	Lifestyle modification for weight reduction through diet and increased physical activity is indicated for obese patients (BMI is $\geq$30)	NCEP ATP-III, 2002	III	Fair	B
3	Individualize drug therapy for modification of insulin resistance or dyslipidemia in the presence of metabolic syndrome using clinical judgment	Working Group Consensus	III	Poor	I

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

X. Reschedule Lipids Evaluation at Appropriate Time and Follow Up to Maintain Goals

Objective

Measure the efficacy of prescribed therapy for hyperlipidemia after allowing sufficient time to reach a new steady state.

Recommendations

1. Lipid profiles should be reevaluated after at least 6 to 12 weeks of drug therapy or change in dose or after at least three to six months of dietary therapy to document efficacy, identify adverse effects, and to titrate medication dose. [I]
2. Follow-up visits should [I] include:
    - Patient history

- Physical exam
- Laboratory tests
- Documentation of adverse events

3. Once the goal is achieved, therapy for dyslipidemia should be continued to maintain the goal. Treatment of dyslipidemia is a lifelong process; however, adjustments may be necessary if the patient develops medical conditions that affect the severity of comorbidity or life expectancy.

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Reevaluate serum lipids after at least 6 to 12 weeks of therapy or after at least three to six months of TLC	Working Group Consensus	III	Poor	I
2	Follow-up visits should include: patient history, physical exam, lab tests, and adverse event documentation	Working Group Consensus	III	Poor	I

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

Y. Follow Up, Repeat Lipid Evaluation At Least Annually

Objective

Ensure that patients initially treated for dyslipidemia receive periodic reassessment of the efficacy of treatment.

Recommendations

1. Lipid evaluations should be repeated at least annually. [I]

	Recommendation	Sources of Evidence	QE	Overall Quality	R
1	Perform periodic follow up	NCEP ATP-III, 2002	III	Poor	I

QE = Quality of Evidence; R = Strength of Recommendation (see Appendix A in the original guideline document)

Definitions:

Strength of the Recommendations

A: A strong recommendation that the clinicians provide the intervention to eligible patients.
Good evidence was found that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.

B: A recommendation that clinicians provide (the service) to eligible patients.
At least fair evidence was found that the intervention improves health outcomes and concludes that benefits outweigh harm.

C: No recommendation for or against the routine provision of the intervention is made.
At least fair evidence was found that the intervention can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.

D: Recommendation is made against routinely providing the intervention to asymptomatic patients.
At least fair evidence was found that the intervention is ineffective or that harms outweigh benefits.

I: The conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention.
Evidence that the intervention is effective is lacking, or poor quality, or conflicting and the balance of benefits and harms cannot be determined.

	Net Benefit of the Intervention			
Quality of Evidence	Substantial	Moderate	Small	Zero or Negative
Good	A	B	C	D
Fair	B	B	C	D
Poor	I	I	I	I

Quality of Evidence

I: At least one properly done randomized controlled trial

II-1: Well designed controlled trails without randomization

II-2: Well designed cohort or case-control analytic study, preferably from more than one source

II-3: Multiple time series evidence with/without intervention; dramatic results of uncontrolled experiment

III: Opinion of respected authorities, descriptive studies, case reports, and expert committees

Overall Quality

Good: High grade evidence (I or II-1) directly linked to health outcome

Fair: High grade evidence (I or II-1) linked to intermediate outcome; or moderate grade evidence (II-2 or II-3) directly linked to health outcome

Poor: Level III evidence or no linkage of evidence to health outcome.

Net Effect of Intervention

Substantial:

- More than a small relative impact on a frequent condition with a substantial burden of suffering, or
- A large impact on an infrequent condition with a significant impact on the individual patient level

Moderate:

- A small relative impact on a frequent condition with a substantial burden of suffering, or
- A moderate impact on an infrequent condition with a significant impact on the individual patient level

Small:

- A negligible relative impact on a frequent condition with a substantial burden of suffering, or
- A small impact on an infrequent condition with a significant impact on the individual patient level

Zero or Negative:

- Negative impact on patients, or
- No relative impact on either a frequent condition with a substantial burden of suffering, or
- An infrequent condition with a significant impact on the individual patient level

Abbreviations and Acronyms List

ACS – acute coronary syndrome

AIDS – acquired immune deficiency syndrome

ALT – alanine aminotransferase

AST– aspartate aminotransferase

AMI– acute myocardial infarction

BMI – body mass index

CAD – coronary artery disease

CHD – coronary heart disease

CK – creatine kinase

CV – cardiovascular

CVA – cerebrovascular accident

CVD – cardiovascular disease

DM – diabetes mellitus

HbAlc – glycosylated hemoglobin A1C

HDL-C – high density lipoprotein cholesterol

HIV – human immunodeficiency virus

HsCRP – high sensitive C-reactive protein

HTN – hypertension

LDL-C – low density lipoprotein cholesterol

LFT – liver function tests

MI – myocardial infarction

MNT – Medical Nutrition Therapy

PUD – peptic ulcer disease

SCr – serum creatine

TC – total cholesterol

TG – triglycerides

TLC – therapeutic lifestyle change

TSH – thyroid-stimulating hormone

CLINICAL ALGORITHM(S)

Algorithms are provided for:

- Screening
- Initiation of Therapy
- Follow-up of Therapy

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The majority of the literature supporting the science for these guidelines is referenced throughout the original guideline document and is based upon key randomized controlled trials and longitudinal studies published from 1999 through 2004.

Where existing literature was ambiguous or conflicting, or where scientific data was lacking on an issue, recommendations were based on the clinical experience of the Working Group. These recommendations are indicated in the evidence tables as based on "Working Group Consensus." A complete bibliography is provided at the end of the document.

The quality of the evidence supporting individual recommendations is given for selected recommendations (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Dyslipidemia is a major risk factor for coronary heart disease and atherosclerotic cardiovascular disease and its subsequent morbidity and mortality. Lipid-related interventions, including lifestyle modifications, such as diet and exercise, and drug therapy can reduce the risk of atherosclerotic cardiovascular disease in patients with high cholesterol.

POTENTIAL HARMS

- Potential adverse effects and precautions for drug therapy used in dyslipidemia are provided in Appendix E-1 and E-3 of the original guideline document.
- There are significant drug interactions noted with bile acid resins, fibrates, niacin, and statins. See Appendix E-2 in the original guideline document for a list of known drug interactions to date.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Statins are contraindicated in active liver disease, in those persons with persistent elevation of liver transaminases, and in pregnancy.
- Niacin is contraindicated in hepatic disease and relatively contraindicated in gout or history of complicated/active peptic ulcer disease (PUD). Use niacin with caution in patient with diabetes, since it may alter glucose control.
- Fibrates are contraindicated in severe renal or hepatic disease, including primary biliary cirrhosis and preexisting gallbladder disease.
- Refer to Appendix E-1 and E-3 of the original guideline for additional information on contraindications.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Although this guideline was developed for a broad range of clinical settings, it should be applied with enough flexibility to accommodate local practice and individual situations.
- Specific recommendations for the management of lipid disorders in those with metabolic syndrome have been described in recent national guidelines (National Cholesterol Education Program Adult Treatment Panel III [NCEP ATP-III]). The recommendations emphasize lifestyle management (weight loss, physical activity, dietary fat restriction). Medications can potentially favorably alter low levels of high-density lipoprotein (HDL) and high levels of triglycerides (TG) and in theory reduce the risk of cardiovascular disease in individuals with metabolic syndrome. However, specific treatment targets and recommendations have not been fully clarified, particularly with regards to drug therapy, largely on the basis of a lack of hard outcomes data from clinical trials. Further clinical trial data will be required before more specific recommendations can be made regarding the treatment of low level of HDL and high level of TG in metabolic syndrome. These issues will be addressed in detail in future revisions of the guidelines as more definitive data become available.
- Although this guideline represents the best evidence-based practice on the date of its publication, it is certain that medical practice is evolving and that this evolution will require continuous updating of published information. In addition, the reader is reminded that this document is intended as a guideline and can never supersede the clinical judgment of the healthcare provider.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The Veterans Health Administration (VHA) instituted performance measures for implementation of clinical practice guidelines in fiscal year 1998. These measures included screening for lipid abnormalities in diabetic patients with established coronary heart disease. Along with the work in the current guideline itself, both the Veterans Health Administration and the Department of Defense (DoD) are developing additional performance measures.

IMPLEMENTATION TOOLS

Clinical Algorithm
Pocket Guide/Reference Cards
Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Management of Dyslipidemia Working Group. VA/DoD clinical practice guideline for the management of dyslipidemia. Washington (DC): Department of Veterans Affairs, Department of Defense; 2006. 140 p.

ADAPTATION

This guideline drew heavily from the following sources:

- Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on the detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). Journal of the American Medical Association 2001, 285 (19), 2486-2497.
- NCEP ATP-III, 2002: Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002, 106, (25), 3143-421.
- The U.S. Preventive Services Task Force Guide to Clinical Preventive Services. Second Edition 2001.
- Pharmacy Benefits Management—Medical Advisory Panel. The pharmacologic management of hyperlipidemia. VHA PBM-SHG Publication. Hines, IL: Pharmacy Benefits Management Strategic Health Group, Veterans Health Administration, Department of Veterans Affairs

DATE RELEASED

2001 Dec (revised 2006)

GUIDELINE DEVELOPER(S)

Department of Defense - Federal Government Agency [U.S.]
Department of Veterans Affairs - Federal Government Agency [U.S.]
Veterans Health Administration - Federal Government Agency [U.S.]

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

The Management of Dyslipidemia Working Group

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

ENDORSER(S)

Veterans Health Administration National Clinical Practice Guideline Council - Federal Government Agency [U.S.]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Veterans Health Administration, Department of Defense. VHA/DoD clinical practice guideline for the management of dyslipidemia in primary care. Washington (DC): Veterans Health Administration, Department of Defense; 2001 Dec. Various p.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Department of Veterans Affairs (VA) Web site.

Print copies: Available from the Department of Veterans Affairs, Veterans Health Administration (VHA), Office of Quality and Performance (10Q), 810 Vermont Ave. NW, Washington, DC 20420.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Diagnosis and management of dyslipidemia guideline summary – update 2006. Washington (DC): Department of Veterans Affairs (U.S.); 2006. 25 p.
- Diagnosis and management of dyslipidemia pocket guide – update 2006. Washington (DC): Department of Veterans Affairs (U.S.); 2006. 2 p. See the related QualityTools summary.
- Diagnosis and management of dyslipidemia key points card – update 2006. Washington (DC): Department of Veterans Affairs (U.S.); 2006. 2 p. See the related QualityTools summary.

Electronic copies: Available from the Department of Veterans Affairs (VA) Web site.

Print copies: Available from the Department of Veterans Affairs, Veterans Health Administration (VHA), Office of Quality and Performance (10Q), 810 Vermont Ave. NW, Washington, DC 20420.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on August 9, 2002. The information was verified by the guideline developer on September 25, 2002. This NGC summary was updated by ECRI on November 7, 2006.

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